

Kiagawa *et al.*, (WO 98/08975). Reconsideration of the claims in light of the amendments presented above and remarks that follow is respectfully requested. Support for the amendments to Claim 9 can be found in the specification at page 14, lines 23-32. The changes to the specification and the claims are contained in the page entitled “Version Showing Changes Made.” An Appendix of Pending Claims, which reflect the claims after entry of this amendment, is attached for the Examiner’s convenience.

#### The Specification

The specification stands objected to for containing an embedded hyperlink. As the embedded browser code has been removed by the amendment to the specification presented above, withdrawal of the objection is respectfully requested.

#### 35 U.S.C. § 112, second paragraph

Claims 9-16 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. In particular the Examiner asserts that Claim 9 is indefinite as unclear whether the recited complex or merely the presence of the complex is detected. As shown above, Claim 9 has been amended to recite more clearly what the applicant regards as the invention. Accordingly, withdrawal of this rejection is respectfully requested.

The Examiner also asserts that Claim 9 is indefinite for the recitation “detecting the presence of said assay complex as an indication of the presence of said target of said target sequence” because “indication” is a non-specific relational phrase. As shown above, Claim 9 has been amended to recite more clearly what the applicant regards as the invention. Accordingly, withdrawal of this rejection is respectfully requested.

#### 35 U.S.C. § 102(e)

Claims 9, 10, and 12-14 stand rejected under 35 U.S.C. §102(e) as being anticipated by Drmanac *et al.* An anticipation rejection requires that a single reference expressly or inherently disclose each and every element of a claim. *In re Paulsen*, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); MPEP § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir.

1989). Claim 9, and thus all claim depending from Claim 9, recites a method wherein the capture probe has been coated with a recombinase prior to contacting the target with the capture probe. As Drmanac *et al.* does not recite such pre-coating, it therefore does not recite each an every element of the claim. Accordingly, withdrawal of this rejection is respectfully requested.

35 U.S.C. § 103(a)

Claims 9-16 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Kiagawa *et al.* in view of Drmanac *et al.* When rejecting a claim under 35 U.S.C. § 103, the Examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Bell*, 26 USPQ2d 1529 (Fed. Cir. 1993). To establish a *prima facie* case, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify or combine the reference teachings in the manner suggested by the Examiner. M.P.E.P. § 706.02(j).

The Examiner has stated that the motivation to immobilize the probes of Kiagawa *et al.* onto the solid support of Drmanac *et al.* is “to provide a reusable array of capture probes for the obvious benefit of economy of reusable components.” (7/9/02 Office Action, page 6). However, such a combination would defeat the purpose of the invention disclosed in Kiagawa *et al.* and if a proposed modification would render the prior art invention unsatisfactory for its intended purpose, there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 221 USPQ 1125 (Fed. Cir. 1984). Unlike Drmanac *et al.*, Kiagawa *et al.* makes use of unlabeled heterologous probes and labeled homologous probes. By including heterologous probes Kiagawa *et al.* has been able to greatly increase “the specificity of targeting, enriching, detecting and isolating of a target nucleic acid sequence.” (See Kiagawa *et al.* page 15, lines 30-31). Key to the use of these heterologous probes is the ability to separate them away from the homologous probes after incubation with the target. The combination suggested by the examiner would defeat the purpose of the invention disclosed in Kiagawa *et al.*, as the heterologous probes would be immobilized to the solid support of Drmanac *et al.* and incapable of separation from the homologous probes. As there is no motivation to combine these two references, Applicant respectfully requests withdrawal of this rejection.

Claims 11, 15 and 16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Drmanac *et al.* in view of Kiagawa *et al.* As discussed above, the examiner cannot provide motivation to combine these two references, since the proposed combination would render Kiagawa *et al.* unsatisfactory for its intended purpose. Accordingly, Applicant respectfully requests withdrawal of this rejection.

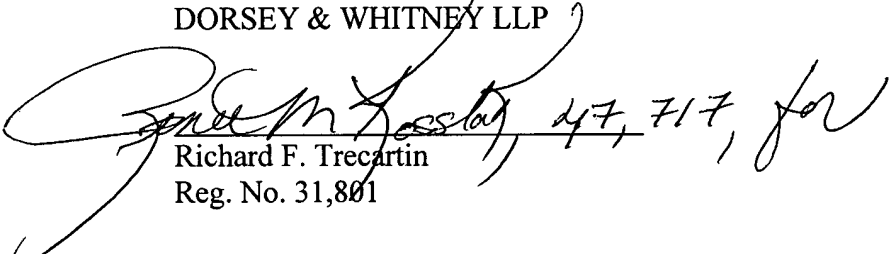
#### CONCLUSION

On the basis of the amendments and remarks presented herein, Applicants believe that this application is now in condition for immediate allowance. Applicants respectfully request that the Examiner pass this application to issue, and early notice of such is requested. This paper is filed under 37 C.F.R. section 1.34(a).

Respectfully submitted,  
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Date:

1/9/03

  
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## VERSION SHOWING CHANGES MADE

### In the Specification:

The paragraph beginning at Page 8, Line 18, has been amended as follows:

---In a preferred embodiment, the secondary label is a binding partner pair. For example, the label may be a hapten or antigen, which will bind its binding partner. In a preferred embodiment, the binding partner can be attached to a solid support to allow separation of extended and non-extended primers. For example, suitable binding partner pairs include, but are not limited to: antigens (such as proteins (including peptides)) and antibodies (including fragments thereof (FABs, etc.)); proteins and small molecules, including biotin/streptavidin; enzymes and substrates or inhibitors; other protein-protein interacting pairs; receptor-ligands; and carbohydrates and their binding partners. Nucleic acid - nucleic acid binding proteins pairs are also useful. In general, the smaller of the pair is attached to the NTP for incorporation into the primer. Preferred binding partner pairs include, but are not limited to, biotin and streptavidin, digoxin and Abs, and Prolix™ reagents (see [www.]prolixinc.com /ie4/home.html).---

### In the Claims:

9. A method of detecting [the presence of] a target sequence in a sample comprising:

(a) providing a substrate comprising an array of capture probes coated with a recombinase;

(b) contacting said target sequence with said array, [wherein either said capture probes or said target sequence is coated with a recombinase, to form an assay complex,] to form an assay complex; and

(c) detecting [the presence of] said assay complex [as an indication of the presence of] to detect said target sequence in said sample.

10. A method according to claim 9 wherein said recombinase is a recA recombinase.

11. A method according to claim 10 wherein said recA recombinase is E. coli recA.

12. A method according to claim 9 wherein said capture probes comprise said recombinase.

13. A method according to claim 9 wherein said target sequence comprises said recombinase.

14. A method according to claim 13 further comprising coating said target sequence with said recombinase.

15. A method according to claim 9 wherein said target sequence is RNA.

16. A method according to claim 15 wherein said RNA is coated with a recombinase.